Myeloma Matters: A Podcast Series from the Multiple Myeloma Research Foundation

Episode 6: Relapsed/Refractory Multiple Myeloma

Transcript

Mark Herkert: I was very realistic. I, you know, I had, I thought two years was like, cartwheels. Two years is like, unicorn rainbows, you know? That was like, that was really good. So yeah. I knew it was going to come back. And I was just hoping to get a couple of years. So I, I achieved that, and I was happy with that. Um, I you know, no one's happy to relapse. But I was fully prepared for that. As much as you can be.

Narrator: Welcome to the *Myeloma Matters* podcast, hosted by the Multiple Myeloma Research Foundation—focusing on patients' experiences with and perspectives on multiple myeloma topics that matter to anyone affected by this blood cancer.

In this episode, we tackle the difficult topic of what happens when a patient's treatment doesn't work or stops working. You'll hear from three patients who've faced this situation and learn how they navigated the stressful process of making decisions about their treatments, including how they approached discussions with their health care team to determine the best plan for this new stage of their diagnosis.

Please note that every myeloma patient is unique; the information in this podcast is not intended to replace the services or advice of trained health care professionals. Please consult with your health care team or contact the M-M-R-F Patient Navigation Center at 1-888-841-6673 if you have specific questions about your health.

Also, if you'd like to support this podcast series, we'd love for you to leave a comment or review wherever you get your podcasts.

When myeloma patients receive their first line of therapy—that is, their initial therapy after they've been diagnosed with myeloma—the goal is for the treatment to induce a long period of remission. Unfortunately, some patients don't respond to this initial treatment; their myeloma is considered resistant, or *refractory*, to the treatment.

Even patients who do respond are likely to eventually experience a return of the disease, also known as a *relapse*. Multiple myeloma is a chronic disease that is characterized by several cycles of remission and relapse.

Relapse can be described in one of two ways. In a *clinical* relapse, the patient experiences new or returning symptoms, such as bone pain or kidney problems. More commonly, however, myeloma returns as what is called a *biochemical* relapse. This happens when a patient has no symptoms, or perhaps only mild symptoms, but is found to have indicators of myeloma—for example, M protein—in the blood or urine.

This was the case for our first guest, David Franks, who was diagnosed with multiple myeloma in 2016. Shortly after receiving his diagnosis, David started induction therapy followed by an autologous stem cell transplant. He initially responded well to his transplant and had planned to enroll in a maintenance therapy clinical study. When he went in for screening for the study, however, his blood work revealed that his myeloma was back.

David Franks: And it was back with a vengeance. I had – I did not feel bad at that point, I had no real pain going on, no new pain. But it was back heavily.

To catch relapse early, it's important for patients to continue seeing their doctor regularly—even when they're in remission. Keeping up with regular visits gives the health care team the opportunity to conduct the blood tests or imaging tests that can provide the first signs of returning myeloma.

For Mark Herkert, who you heard from at the top of our program, it took two stem cell transplants to get a response after his diagnosis. Mark's remission lasted 2 years, at which point signs of returning myeloma appeared in his bloodwork. He was started on a high dose of Revlimid, which helped him achieve another 2-year remission. But his myeloma returned again.

Mark Herkert: And then that started to wane, and, then I blew through several therapies really fast.

Our final guest, John Busch, was first diagnosed with smoldering myeloma in 2006. After 3 years of monitoring his bloodwork, John's health care team decided to initiate treatment. He received induction therapy with Revlimid, Velcade, and dexamethasone, but opted not to get a stem cell transplant at that time. Over the next several years, John went on and off a variety of therapeutic regimens that helped him achieve and re-achieve remission. Following one of his relapses, John's health care team recommended that he enroll in a clinical study for treatment with a new drug.

John Busch: So they put me in the clinical trial for that. They thought I could – yes, let's see how that goes. Even though I had responded to every previous treatment pretty much pretty well, this was a dud. It was surprising and kind of a little bit disconcerting, but in a fundamental way.

It's like sometime when you have an experience that shakes your world view a little bit. So I realized that I had been operating with this sense that treatment is gonna work for me. It's just gonna keep working. Then when this one didn't work and it's touted as the immunotherapies. This is a new frontier. It's gonna change everything, blah, blah, blah. Doesn't work for me. Then I really had – it shook me and so all of a sudden I came around to stem cell transplant.

There are many effective treatments available for relapsed or refractory myeloma, with more being tested in clinical studies all the time. These treatments can help patients get their disease back to a place where they are able to continue with their everyday lives.

When choosing a therapy at relapse—whether it's the patient's first relapse, second relapse, or more—doctors take into consideration a number of factors, including the patient's disease features, treatment history, medical history, and treatment preferences.

Disease-related factors that may influence treatment include considerations such as the genetics of the patient's myeloma and the pattern of relapse. David was initially diagnosed with a high-risk form of myeloma, characterized by a chromosomal abnormality that increased his likelihood for relapse. This may have been the reason he relapsed so quickly after his stem cell transplant, and it suggested to his health care team that he may need a more aggressive form of treatment.

A patient's treatment history can also help doctors determine what medications to try or to avoid. This can include what treatments have or haven't already been tried, as well as what side effects the patient may have experienced with prior therapies. John, for instance, experienced peripheral neuropathy from his Velcade treatment, which meant that that agent should be avoided in future treatments.

John Busch: I routinely warn new patients, if you go on Velcade you've got to be so vigilant about paying attention to all the little things. So most people, I'm in that camp, don't – they're not paying attention to every little thing that's going on in their body. We're not really trained that way and that's not how we are in this modern age where we're tuned into the body and all the subtleties of the things that are happening.

John also hadn't received a stem cell transplant as part of his initial treatment, which meant that he could get one later after his disease relapsed.

The patient's preferences and needs can also influence what treatments are considered after relapse. These include other health problems a person may

have—such as heart problems or diabetes—and how treatment will affect a person's lifestyle.

Patients are encouraged to take part in their treatment decision-making and to communicate their preferences. Both John and Mark wanted less-intensive approaches to their treatments. They communicated those preferences to their health care teams and advocated for drug holidays following some of their treatments.

Mark Herkert: They wanted to get me on Rev and I thought, I've only got so many bullets in my gun. And, I don't want to blow through that one when it's not pressing right now. I, the myeloma's under control and, I, I wanted to push out the Rev as long as possible. So for two years, I did zip. I didn't do anything. And, that was great.

John Busch: It's funny. My doctor, we have this mutual, respectful, but sometimes borderline combative relationship. At least it was like that in the early days. I think – I don't know. I think we came – he seemed to eventually accept. I remember him bringing in a medical fellow to the appointments. Frequently he's bringing in somebody. He said – one of the times he said to the fellow, "This is the patient who tells us what we're going to do." So yeah. I was very pretty – I was very emphatic about what I wanted, what I didn't want and so forth. So yeah. Now I don't even think he tries to – in fact, he's looking for opportunities to not only accommodate, but help me have drug holidays. Even though he's definitely in the camp of beat it down and keep it down. So but still we're muddling along.

Different types of therapies are available for relapsed or refractory multiple myeloma based on the number of treatments a patient has received. Some treatments can be used for patients who've had three or fewer therapies, who are said to be in the *early relapse* stages. Currently, other treatments, such as immunotherapies, are reserved for patients who've received more than three therapies.

Treatments for early relapse myeloma are frequently given in a combination regimen—that is, two, three, or even four drugs administered together as part of a treatment plan. For instance, a monoclonal antibody—such as Darzalex or Sarclisa—may be given alongside an immunomodulatory drug—such as Revlimid or Pomalyst—or a proteasome inhibitor—such as Velcade or Kyprolis—along with a steroid. There are other drug combinations that include a drug in another class called Xpovio, too.

The combination of drugs chosen for one patient's relapse may be different from those used for another patient when considering their risk factors, treatment

history, and preferences. Indeed, David, Mark, and John have all received some combination of these drug classes for their relapse, but the approaches have been individualized based on their specific needs.

After the third line of therapy, patients who relapse are more likely to have been exposed to the three main classes of drugs previously mentioned—monoclonal antibodies, immunomodulators, and proteasome inhibitors. At this point, they may no longer respond to these types of agents. These patients are what are known as triple-class refractory. Treatments for these patients include targeted immunotherapies, which include CAR T-cell therapies and bispecific antibodies. A CAR T cell is a modified T cell. These are generated from a patient's own white blood cells, taken from their body and genetically engineered to express a protein that helps them bind and kill myeloma cells. Because CAR T cells are engineered from a patient's own cells, the treatment process requires many steps and takes time, typically 4 to 6 weeks.

CAR T-cell therapy has the advantage of being a one-and-done approach, meaning that it doesn't need to be given regularly or continuously. Two CAR T-cell therapies are currently approved by the FDA: Abecma and Carvykti. Bispecific antibodies are similar to CAR T cells in that they bring a patient's own T cells in close contact with myeloma cells to promote myeloma cell death. One component of the antibody binds to C-D-3—a protein on the surface of cancer-killing T cells—and the other side binds to a specific protein on the surface of myeloma cells. Bispecific antibodies don't require a lengthy process to develop and prepare for individual patients. Any patient can get them immediately if they need it. This is considered an off-the-shelf treatment. However, bispecific antibodies are given regularly over time, typically every week or every 2 weeks; it is not a one-and-done treatment.

Three bispecific antibodies have now been approved for treatment of relapsed or refractory multiple myeloma: Tecvayli, Talvey, and Elrexfio.

Immunotherapies such as CAR T cells and bispecific antibodies are typically given on their own rather than as part of a multi-drug regimen. For more information on these therapies, our episode on *Targeted Immunotherapy* goes into detail about these options for heavily pretreated myeloma patients. Clinical studies are also available across all stages of myeloma treatment. Participation in a clinical study is not just for patients who are running out of options. For instance, David was in the early phases of enrolling in a clinical study for maintenance therapy after his stem cell transplant before his myeloma relapsed.

A clinical study gives patients the opportunity to potentially receive a form of treatment they wouldn't otherwise be able to receive. Myeloma research has evolved dramatically over the past two decades, with many new drugs becoming

available. Bispecific antibodies and CAR T cells have become newly available just within the last couple of years, and these innovations are the products of extensive research and clinical studies.

John enrolled in a clinical study of a new drug after his myeloma relapsed, which unfortunately did not induce a response for him. Patients who don't respond to treatment during a clinical study may choose to explore another treatment option instead.

Participation in a clinical study is always voluntary. No patient is expected to be a "guinea pig" for research. Cancer research and clinical studies are under very tight supervision and are held to very high standards. Doctors may encourage their patients to consider a clinical study, but patients are never obligated to participate or even continue participating after they begin.

David Franks: One, I trust my doctors that they wouldn't – if this or for a clinical trial, they would not – obviously, and especially with all the rules and regulations regarding clinical trials, they don't just throw you in just to throw you in. You have to meet certain criteria. I think again, my health overall gives me that strength to handle whatever they might want to trial me on. Again, also my background, knowing what clinical trials truly can accomplish I'm wide open for it. If they presented it to me. I probably wouldn't go in say, hey, I want to be part of this trial. But if they presented a proper one that I would be a good candidate for, I would happily do it.

To learn more about clinical studies and why they're important to patients who have multiple myeloma or one of its precursor conditions, our episode on *Clinical Studies* shares the experiences of three patients who have participated in clinical studies and the steps they took to enroll.

The treatment landscape for relapsed and refractory multiple myeloma is rapidly growing, with many options for patients. The continually expanding list of options offers hope to Mark.

Mark Herkert: Because honestly now, I mean, when you get diagnosed, they don't really tell you oh, you've got X number of years to live, because they don't know. The needle just keeps getting pushed. People are living longer. They don't, they don't even know now. I mean, because there's so many new things. So, and that's good. That's good, not to have like a number thrown at you.

Treatment approaches are tailored based on a variety of personal factors, including how long a patient has been in remission, how they've responded to previous treatments, and what kind of therapies they've received.

To learn more about the process of treating relapsed or refractory multiple myeloma, let's turn now to Mark, John, and David, who join the MMRF's Mary DeRome to share their perspectives and experiences with relapse over the course of their disease, how they and their doctors approached treatment decisions, and how they coped with the news of their relapse.

Multiple myeloma patients Mark Hercart, John Bush, and David Franks join the MMRF's Mary DeRome to share their perspectives and experiences with myeloma relapse, how they and their doctors approached treatment decisions, and how they coped with the news of their relapse.

Mary DeRome (MMRF): We're going to talk about how it feels to undergo relapse once you've gone through your newly diagnosed phase.
Being diagnosed with multiple myeloma in and of itself is an overwhelming prospect, so I want to talk to each of you about the impact of learning that your myeloma had relapsed after your initial treatment. Did you feel like you were prepared for this, considering that myeloma is an incurable cancer?
John, let's start with you.

John Bush: I've been at this for now 17 years, so I frankly can't remember my initial relapse. I'm not even sure when or what it was, because I've tended to follow a course that's maybe a little nonconventional, which is to seek and go on drug holidays. Initially, maybe, I had a little fantasy that my drug holiday would extend for a long period of time. I always expected it to come back.

And it has. That's usually the end of the drug holiday, when things are relapsing, and I go, "Well, that was fun, but I've got to jump back in," and then go back in. I've done that a number of times.

Mary DeRome (MMRF): Dave, what about you? How did you feel when you found out you had relapsed?

David Franks: Well, mine was very short, within 90 days of my stem cell transplant. It was 2017. I had my transplant that February, and by the middle of April it was raging again. To get through the stem cell transplant and to feel good afterwards—to finally get past all the recovery and start feeling good again, feeling like "All right, we can just go on maintenance and beat this and just carry on with my life." To have that, and then to relapse, it was almost a feeling of failure, like "What did I do?"

Did I do something to allow it to come in? Did I not take my medicine right? Since then—it's been 6, 7 years now—I've realized it wasn't. It just happens. To have that mentality, then, to switch to a mindset of, "It can just happen no matter what you do," it actually helped prepare me for when it does happen again. Whatever

else is out there that they want to give you for medications that's new and the latest and greatest, go for it.

Mary DeRome (MMRF): Mark, tell us about how it went for you when you learned that you had relapsed.

Mark Hercart: Similar to John, I had also taken myeloma holidays—the road less traveled. Similar to Dave, my first transplant didn't work. I in essence wound up doing a tandem, which is not how we planned it; it's just how it worked out. So I would say that the first year of my treatment did not go particularly well, and I was not in a great place, because I didn't really have any victories. I was just getting my ass kicked. I didn't feel good about the future.

Once the second transplant worked and I took a holiday, my outlook changed. I started to look at this more as a chronic condition as opposed to a death sentence. I realized early on that this was an emotional rollercoaster, because you'd be waiting for the results to get back and either they were promising or it was going to be, “Nope, things aren't working.” And I was like, “Man, I've got to get off this thing, because there are just too many highs and too many lows.” To try to even that out, I just tried to take a long-term approach, which is that some days I'm going to get good news, some days it's not going to go the way I planned, but I'm just not going to get too high and I'm not going to get too low. That's really helped smooth things out. That's what I needed for my peace of mind. People say, “Oh, I'm in remission.” I never use that word, “remission,” because that to me implies that I could beat myeloma. And I don't think that's ever going to happen. Maybe with some of the new CAR T-cell and bispecific stuff. Maybe. Myeloma ultimately has the upper hand in this day and age that we find ourselves.

I try to stay away from terms like “remission,” because those are just setups for me. The flip side of that is the disappointment at relapse. I just don't want to set myself up like that.

Mary DeRome (MMRF): Let's talk about choosing your next line of therapy after relapse.

John, I know that you've relapsed a number of times. Each time you relapse, how do you discuss this happening with your care team, and how do you discuss with them what the next potentially right treatment might be for you?

John Bush: In the early days, there seemed to be counseling from the myeloma docs at the seminars that you wanted to have this game plan in place with this long-term perspective, almost like you were going to line up all the treatments way ahead of time, have them in mind, and have it all laid out with your doctor. I mean, I actually thought, “How could you do that?” because it's all changing.

It turns out that my oncologist definitely doesn't want to do that. I've been with him a long time, and we have a good understanding, but the way that it works with him is that when I've been on something for a while and then prod him about what might be next, he asks, “What are you thinking about? Do you have anything in mind?” He doesn't really want to give me much advance notice, because he wants to maintain full flexibility to introduce the best option right in the moment. And I appreciate that, because I'll bet some people—like me—might get a little fixated on what that next thing is and then maybe be taken aback if something else is recommended at the moment that I really feel the need to go into the next thing.

I'm okay with it. But at a certain point I do want to have some idea so I can bone up on treatment and have the questions that I want to pose in mind. That's how it's gone. Because of all the activity in the myeloma area, there has always been something pretty promising that I've been able to step into.

I would say the thing that's also helped—harkening back to the previous question about relapse and the emotional impact of it—is that I have had pretty good responses, and so I have some confidence about something working. I don't worry about it too much. We start something, and we just go along.
That's how we have handled it thus far, and so far, so good.

Mary DeRome (MMRF): Did you say you were diagnosed 19 years ago?

John Bush: Seventeen years ago.

Mary DeRome (MMRF): Back then, there weren't a lot of choices, but things have changed in myeloma since then. Now there are a lot of things that people can be put on, and some of these new immunotherapies are amazing. Now, whenever you go to these major meetings and they talk about these new therapies, doctors are starting to talk about cures. We're headed in the right direction with all these new therapies. It's still always just a big decision to determine what to go on next after you relapse.

Dave, how have you handled that with your care team?

David Franks: Well, to go off of what John was saying, you don't want to get too focused on one thing. And, like him, I've had a great response to when I relapsed right after my stem cell transplant. I responded well with Revlimid for induction, so they wanted me to stay on that and then add Darzalex. I've had a great response to that for the last 6 years or so. It's one of these “Don't rock the boat” situation, along with what John was saying: I'm not going to focus on “Oh, well, this one's just come out...,” because if I continue to have a good response, that one may be pushed off to the side, or it won't be the right fit for me where it would be the right fit for somebody else.

Naturally, you stay up on what is new, what the current treatments are for any of us who relapse. Until it happens, you can stay current, but you should never really focus on it and obsess over “Well, are we going to go this way or this way?” I just trust my team. I am with my local oncologist, and I have a specialist out at Emory. They text; they talk. I trust that they know where I should be. That's really all I can focus on. Otherwise, you're right: you go down a rabbit hole and you worry, “Will this work? Won't it work? How are the side effects?” And that's really all I need to focus on is when it does—because it's not if, it's when. It does relapse. I get my bloodwork every month and you wait that few days for your labs to come back, wondering “Well, is this the month? Is this the month?” At some point, it will be the month that it happens. You've just got to take what they give and readjust to the new medication regimen. I had to adjust to this current one. It took a little while, but it's working out fine, so I have no reason to believe that the next line of treatment won't again get a good response.

Mary DeRome (MMRF): How about you, Mark? When you relapsed and decided on your next therapy with your care team?

Mark Hercart: Well, I am in that boat right now. I've had a partial relapse; for the first time, my myeloma has come back in a very specific part of my body. I just went through a couple weeks of radiation, which is a new experience. I'm still on the same therapy, which is similar to Dave’s: daratumumab. I've had a very deep response, 6½ years now, which has been an amazing run. I knew that it's not going to last forever. And as the years went by on daratumumab, I was like, “Man, this is just the gravy train, because this is such a long response.” I've been thrilled with how successful it's been with minimal side effects.
But I knew it was going to fail at some point, that the myeloma would adapt, as it always does.

I'm still on daratumumab. I'm waiting to see if the radiation worked. To me, it's a harbinger, that fact that we may be coming to the end days of daratumumab for me. Fortunately, it's been an elongated process, so I haven't had to make any sudden decisions. I've had a while to let it sink in and grieve for the potential loss of daratumumab, which has been my buddy for a while now.

You can think, “I know this is coming,” but when it happens, it can still be a difficult adjustment, because it's a lifestyle change. There are going to be side effects. You're going to be very closely monitored. Your leash is going to be short. It's just going to be very disruptive in terms of your lifestyle. Unfortunately, that's just part of the game with myeloma.

Mary DeRome (MMRF): Let's talk about these side effects. You mentioned that you're on daratumumab and you've found it to be pretty good. You haven't had many side effects from it.

Mark Hercart: That's right. It's been amazing. I get cramps, though. I get calf cramps, and I'm a big runner and I stretch and I take electrolytes and I just think it's got to be something with some of the drugs they're feeding me. That's the only real side effect, if I can pin something negatively on daratumumab.

Mary DeRome (MMRF): How about you, Dave. Have you had side effects from anything you've taken since you've relapsed?

David Franks: Mark's the first one that has had the same side effects, cramps. Mine occur right at the soles of my feet. They just cramp up for no good reason. I'm constantly drinking electrolytes, replenishing everything I need, and they still come. It's annoying. It definitely is at the worst times. But it's just that and the fatigue for me.

I've always been high energy. I have no stamina anymore. When I'm working out, I know I have to space things out. It just hits me, and I know when I'm tired and when I'm just done. My wife knows, when I'm tired, to just to keep me moving. When I'm done, she just lets me crash. But that's been the biggest side effect. That took a while to get used to, as somebody who is used to running everywhere.

Mary DeRome (MMRF): John, tell us about side effects you've had with some of the regimens you've been on. Does that have any bearing on the drug holidays that you take? Have you taken those because of side effects?

John Bush: To some degree, yes, just because I feel the drugs. Whatever drug I'm on, I feel it. I remember when I first took Revlimid, which was the first drug that I took. I swallowed the pill and within 15 minutes it's like, "Whoa!" I have something in my system that's a blockbuster!" It's a feeling I've never had. I can feel the power of this drug. I love just feeling normal. Feeling normal is my high. When I'm on any treatment, even though they are—comparatively to other cancers, from what I understand—mild in terms of their side effects, I still feel different. Fatigue for sure. But I don't really feel like myself. I'm some kind of a chemical mix. Part of that, the drug holiday enthusiasm, has been because I just want to feel like myself.

For most of the time I've had dexamethasone in my regimen, and dexamethasone really whacks me—even tiny doses. Right now, I'm on a 4-mg weekly dose, and I feel it. It just whacks me. I hope I don't have to take dexamethasone for the rest of my life.

I love it when I don't have to take dexamethasone, because it puts me through the wringer every week. But anyway, it's part of the reality that we have.

Mary DeRome (MMRF): Let's talk about stem cell transplant. Two of you have had them. We don't hear much from patients who don't initially respond to transplant or who delay their transplant until after relapse. Let's talk about your experiences with stem cell transplant and anything that you may have learned from that experience.

Dave, when you had your transplant, you had a very short response and you relapsed almost immediately. When you talked to your care team about that, what did they tell you? Did they say that it was because your disease was too aggressive? Or was the message that if the stem cell transplant doesn't work, there are other things that could be tried?

David Franks: Both of those. When it did come back, when they retested everything, when they saw those signs, it was back about tenfold over previously when I was first diagnosed. It came back with a vengeance, and I was told, “Well, it can happen.” They weren't floored by it, because people can relapse—even that quickly.

It was something that almost had to be tried. A lot of people and patients nowadays are saying, “Is a stem cell worth it? Should it still be a first line of treatment?” And if I had to do it again, I still would, because you just don't know. I could have had 20 years of remission—there’s that word—but remission from one stem cell transplant. You just don't know until you try it.
I know you didn't ask, but I don't have any regrets for trying it, for doing it. My care team said that, while it can happen, it's just something you have to deal with.

Mary DeRome (MMRF): Mark, let's talk about your experience with transplant. You ended up having two of them. Walk us through what happened there.

Mark Hercart: I did two autologous stem cell transplants. My daughters were 6 and 8 when I was diagnosed, and I didn't like the mortality rate associated with allogeneic transplants. I wasn't willing to roll those dice. Even though I knew the autologous transplants ultimately had a less deep response, I went that route. I got my first one about 6 months after initial diagnosis and a few therapies, and that was pretty much standard protocol where I was being treated. It didn't budge my myeloma numbers once we were finally able to test after a couple of months. They didn't jump, but they didn't go down. It was basically no response.

Then we decided counterintuitively, because I already had enough stem cells stored from when I harvested originally, that we would just roll into a second one. I'm good at pruning trees and climbing trees. I was an arborist, not a myeloma doc, so I deferred to my team.

We went into the second one about 7 months after the first, and then I got a deep 2-year response. That's when I took my drug holiday after doing pretty much back-to-back transplants.

Mary DeRome (MMRF): Talk to us about that. Was it really hard on you to do that physically?

Mark Hercart: It was really tough. I was in the hospital for weeks and both with the Neupogen to stimulate stem cells that—oh, it was the worst, the worst flu, the flu to a factor of ten. It feel like my bones were broken. And once I spiked a fever with the transplant, I was back in. I spent a fair amount of time in the hospital for both. Of course, they didn't have to harvest the second time, so that shortened that cycle. I knew what I was getting into with the first one, so the second one was a little easier in that regard. “Okay, I know the process. I know I'm going to feel like crap. I know my body is going to bounce back.” That was helpful.

For me, the transplants were a little oversold in the sense that the actual success rate in terms of responses is only— I'm going to say only 50% or something. I thought, “Oh, everybody does a transplant, and it's this super arduous process, but it's because it's amazing and it works for almost everyone.” That's not really the case. It still was the protocol at the time. I probably would have done things the same. But I was not aware of the overall effectiveness. The response times are usually, I think, 1 to 2 years, which is a long time for myeloma. But there are very few people that get cured. I know there are people that have had a transplant and that's it and there are no treatment for even decades. But those guys are unicorns.

After my second one—I mean, it takes over your life, right? All the appointments and meetings and how closely they monitor you, and holy smokes. It was a full-time job. That's when I took my holiday. They were like, “Yeah, we recommend maintenance, Revlimid maintenance.” I was like, “Nope. I'm casting off. I'm not going to see you guys for a while. Good luck, and I'll check in at some point.” I got 2 years doing nothing. No maintenance, no dexamethasone, nada. That was fabulous.

My philosophy is, I just have so many magic bullets in my gun. I was like, “You know what? If I got a response and it seems like the transplant is working, I'm not going to go ahead and fire another of my limited number of bullets at myeloma. I want to keep that in reserve until I really need it.”

You have to develop your own philosophy. Most of the time, I'm going to follow the recommendations of my docs, because that's what they do. They study this and all that sort of stuff. Still, I had to have an overarching philosophy, and that helped me make difficult decisions when we hit those crossroads.

I got 2 years out of that, and then I went on Revlimid. Those 2 years were fabulous. I know folks who are on CAR T, and it's basically a drug holiday. When my daratumumab stops working—I mean, at some point—I don't know if it's the next thing. I presume most of us will probably get on CAR T at some point. I'm hoping I get a response and can just cast off.

Mary DeRome (MMRF): Did you run up against any resistance from your care team when you told them that you just wanted to go on a drug holiday and not go on maintenance?

Mark Hercart: They were okay with it. They just gave me the space to make the decisions I needed to make and feel comfortable with. I really appreciated how they respected my autonomy.

Mary DeRome (MMRF): John, your situation is different. You opted to wait to get a transplant. Walk us through that. What was your reason for waiting? If you're approached by a patient who is considering a transplant up front, what learnings from your experience would you convey to that patient?

John Bush: When I was diagnosed and transplant was recommended for me, I recoiled in horror. I was not convinced or persuaded that that was the right route for me.

Particularly in light of the novel treatments that were coming online then and seemed pretty promising, my philosophy became to extend as long as possible with treatment, with relatively benign treatments to just try to treat this gently and just go for the long haul and not go for the home run but go for just managing the disease. That was my orientation.

But I wanted to keep the transplant as an option, so I collected my stem cells at the normal time. But I really hoped that I would never have to do it. I got a lot of pushback from my care team, because they do a lot of transplants and they wanted me to get into one.

I had to hold firm. But they did respect my choice, so we just carried on. At a certain point, it made sense to me to do it. I remained open to it even though I wasn't oriented that way. There was an opening in the door, and then it got to a point where it seemed like maybe I should give it a go—the thinking was that if I wait until I'm a lot older and a lot more decrepit, then maybe it won't actually be an option. At the time, I thought, “Okay, well, I've been through a bunch of treatments now, and maybe this will be a good option now, but in 5 years or 10 years, maybe not. It would be a shame to throw away one of the arrows in my quiver.”

I went for it, and I got the best response of any treatment that I tried previously or since. Would I have gotten that response earlier on and would that have changed the overall course of my disease? I don't know. Since going through the stem cell transplant, I do feel diminished by it, and my blood counts are not what they were before. My body has absorbed a fair amount now of insult and abuse over all this time. I attribute a chunk of that to the stem cell transplant.

I feel actually okay that I waited. It was okay to do it. The research is not really definitive about early versus later transplant. The doctors are not so interested in that question, so they're not really pushing that research too much. But there doesn't seem to be a clear advantage to doing it earlier versus later. I'm glad I didn't put my body through that earlier, but who knows? But I did get a decent response, I think. The clones of myeloma that I have that are active, they're susceptible to melphalan. It seems like that's the reality. Unfortunately, I have to take the old-style cannonball to really get it.

Anyway, I'm glad I did it now. It seems to have had pretty good effect.

Mary DeRome (MMRF): They just finished doing a really large study called the DETERMINATION study on patients who got a stem cell transplant right away versus patients who decided to wait until after they relapsed. What they found, and why transplant is still the standard of care in myeloma, is that the stem cell transplant does offer most people the longest period of progression-free survival when you have it up front. But they've compared the overall survival of these patients who had it up front versus those who had it later, and there really wasn't any difference in most people. There's still some question, but the progression-free survival is worth it for a lot of patients.

Let's talk about clinical studies.

John, were you ever offered a clinical study? Have you been on any clinical trials?

John Bush: I was on one, for Sarclisa. It only sort of worked for me. It was when I had that experience—and my doctors were saying, "Well, probably daratumumab is not going to work any better than that, so even though we haven't tried daratumumab and—maybe daratumumab will work. You don't know." And now, my body is different. I've been through stem cell transplant, et cetera. Maybe it would work now?

But the thinking was "Okay, well, this isn't working. Probably daratumumab is not going to work." that's when I stepped into the stem cell transplant. That was the context for it.

I enjoyed doing the clinical trials. It's interesting to me because I have a science background. Philosophically, I support it and I'm open to doing trials in the future, as well, if anybody wants this heavily treated specimen in their trial.

Mary DeRome (MMRF): Dave, were you ever on a clinical trial or offered to be on a clinical trial?

David Franks: I was offered. I don't know what they were using down at Emory, but there was supposed to be a trial for post stem cell maintenance. I was just about to get started on it when everything came back. I wasn't able to do that. They were looking to try to get me on a trial for relapsed patients, but both doctors agreed that Revlimid-daratumumab would be better to go with, so I wasn't able to start any type of trial.

As far as in the future, like John, I'm all for them. I know the backgrounds with them. I know just how much they have to prove to get through onto trials. If there was one that is right for me, I'll be happy to jump into one if needed.

Mary DeRome (MMRF): Mark, how about you? Have you ever been on a trial or been offered to be on a trial?

Mark Hercart: I was asked to be part of a clinical research study that wasn't directly related to therapies. And I did that. Similar to what Dave was saying, I feel like, as myeloma patients, we have all benefited from past patients who have been willing to do studies. That's the only way that these drugs get approved or that you know they're effective or not. Our success is based upon other people's willingness, so I am totally willing when that point comes. And I suspect it will, because I'm guessing, at some point. My doc talks about CAR T 1.0, and it could still be curative, but it needs to be refined.

Maybe it's not the right way to look at it, but I look at clinical trials as almost hail Marys, when you're out of options. And we all want another day, so I'm sure I'll be willing to go deep on that play.

Mary DeRome (MMRF): That's one good thing about the field: there are always patients who reach the end and they're refractory to everything and the only thing that's suitable for them is something that's in clinical trials.

And patients are like all you guys: They're all interested in participating in these, and this is how we've gotten all of these newly approved therapies so far. And there are so many things that are in the pipeline that are still in trials. You just never know what's going to happen next in this field. It's constantly evolving.

Mark Hercart: I will say that the advantage for me, in my mind, of being treated at a research center is that you do have access to those trials.

David Franks: I totally agree with that. Being an Emory patient as well as local, just the access to any of these research facilities, it's a blessing. You just don't find that in other parts of the world, even in America. There are just areas that are isolated islands, and they don't get access to it unless they're willing to make a lot of sacrifice to travel.

And talk about that leash being short. If you have to go through that—I just don't see how people can do that. But to be near a center like that and like all of us, it's been great.

Mary DeRome (MMRF): Let's talk about family while you're having these treatments and relapses. Dave and Mark, you both had young children at the time when you were diagnosed, so talk about how you were able to let them know about your condition. Were you able to involve them in any aspects of your care?

Dave, let's start with you.

David Franks: My son was 4 when I was diagnosed. At the time, I was in nurse practitioner school and working in neurosurgery. He knew what Daddy did. He always had questions about anything going on at work. When I was diagnosed, we did not hide it from him. We were open with him, as much as you can be with a 4-year-old, with my treatments. He was very attentive to me, saw what I was going through. I could tell he was very scared, and he still has anxiety from it now. He's always asking how I'm feeling. If I get up and I'm aching, he asks, “Are you okay?”

It has affected him. Being honest with him has helped. During my stem cell prep, when I had my central line placed, he was actually wanting to help flush my line, change my dressings with me. He took an active role in that. Then, when I got home from the stem cell transplant, I had no hair. He was with my parents during those 2 weeks so my wife could come down to the hospital and be more with me and present. He got on a FaceTime call with me when I got home the day before he was going to come home.

I wanted to be home for a day just to settle in. And it really, really shocked him to see me without hair. That was the first time I saw him just lose it. But when he got home, I had my hat on and he took it off for me and he was okay with it. But it's been hard with him. Very hard.

Mary DeRome (MMRF): Mark, how about your situation with your kids and your diagnosis?

Mark Hercart: My kids were also young, 6 and 8. Our initial response was to try to protect them, which means shield them from this reality. But everything I read

said, “No, you've got to tell them.” It's hard for me right now to talk about it. My wife and I practiced to try to deliver it in a way that we weren't overwhelmed so we wouldn't scare the kids and do it in an age-appropriate manner. And because they're different kids, they reacted totally differently. One daughter was—you could see she was gut-punched. My other daughter was like “Okay, can I go play now?” They have distinct personalities.

We tried to involve them in the process as much as possible. When I started to lose my hair for the first time, we got out the shaver and they shaved me. They would visit me every day in the hospital during the stem cell transplant. I felt so terrible, but I just didn't want any company except them. I had to see them every day. And they would come in fully gowned up. Eventually they got used to that. It's amazing what you can adapt to, even though it was freaky for them the first time to come into that hospital room, that germ-free environment.

At one point while my older daughter was in high school, she had to do a paper about medical stuff, so she and her friend came with me to an appointment, and they saw what it was like to get my labs drawn and my infusion or whatever I was going through at the time. That was helpful, because as the years go on, it's like, “Yep, got my bloodwork. Everything looks good.” It was this abstract. I didn't look like a cancer patient anymore. They got involved in their things. To be reminded that, yeah, this is still going on was interesting and brought it back home.
I don't hide things from them. They see how I just roll with the punches. It's hard to know what's going through their heads. And they're not kids now; they're young adults. They're in college.

But especially as kids, they haven't learned how to express themselves verbally like we have, even though they're more open in other ways. just checking in with them. We had a lot of family check-ins, little family meetings. “This is what's going on.”

We talked about it a fair amount, because we have used it as a springboard to live life, just suck the marrow out. We go on amazing trips and family vacations, and we spend a lot of time together, the four of us, because we don't take time for granted and we want to make memories. I want to make memories with the kids. That's my legacy. I want them to be able to tell stories to their kids about their granddad.

That's how we flipped the script and have turned it into a positive, by just not taking anything for granted and living large.

Mary DeRome (MMRF): Let's talk about what you see as the next step in your journey and what words of wisdom or encouragement you might give to other patients who are in this relapsed, refractory state of multiple myeloma.
John, I'll start with you.

John Bush: People are still probably being told that everybody's myeloma journey is pretty unique. Everybody's disease and response, their treatment, and so forth is unique. And that sat okay with me and I was comfortable with that. But some people are maybe not so comfortable with that.

Initially, maybe, they're more familiar with other cancers where there's this standard treatment and you go through a standard protocol for a certain standard length of time, and this is quite different. Try to make yourself comfortable with that, as much as you can. I decided I wasn't going to get too hooked on the numbers, but I see a lot of people hang off the numbers of their scan results, their bloodwork. That's hard on you if you're living from test result to test result. I try just to put that out of mind, really, and also just decide not get too hung up on expecting and wanting a certain result and just being more open to whatever comes—however it works out, and then just roll with it. But not try to anticipate too much. Try to just live life as normal as possible and trust that things will work out. And life is just life. Nobody in society is given a certain length of life or quality of life. Your life is your life. It's actually no different in myeloma. Just be okay with that. Embrace that, even though we know we've got something that we think is going to be our demise. But I don't know. I could get hit by a bus this afternoon. That's what I would counsel, is to try to just be in your life, enjoy your life, and not make myeloma a bigger part of it than it really has to be.

Mary DeRome (MMRF): Dave?

David Franks: I spoke at one of the foundations' 5Ks a few years ago, and I still hold onto what I said, one part of it, about when one thing fails there's going to be a next. And then, you know what? There's going to be a next after that. And a next after that. I continue to think of it that way and to just to tie it in with when I was having a stem cell transplant. I was forced by my wonderful wife to get out of bed and walk that mile around the unit every day, whether I wanted to or not. If you just continue to move forward and embrace life—like John said—embrace life, take it day by day, and enjoy it—same with Mark too—and make memories, the myeloma almost goes to the side. That's just a part of it, but it's not you. That goes for anything, not just myeloma. Just continue to move forward and things do work out. You've just got to look at it that way.

Some people say, “Oh, it's too much rainbows and sunshine,” but what's the alternative? Am I going to sit here and wallow in it? Focus on every number? As far as the numbers go, my advice from a nursing standpoint is that you never trust one number. Don't trust that one set of labs that you get. Look for patterns. “Oh, you have a high blood pressure. Okay, let's take it again. You have this. Let's try it again.” When people live that month to month, whatever they're getting for their numbers, trust it but don't trust it. Look at it and go forward from it. See if there's a pattern, then deal with it. It's either deal with it or don't deal with it, and nobody wants to not deal with it. Just take it as it comes.

Mary DeRome (MMRF): Mark?

Mark Hercart: I've heard some people say, “I don't want myeloma to define me.” For me, I mean, it's a big part of my life. It just is. I mean, I'm not going to pretend it isn’t. It takes up a lot of time with doctors' appointments and sometimes, in my headspace, fighting to stay in the day versus projecting out and worrying and all that sort of stuff.

I have tried to embrace it as the new normal. I've gotten involved in support groups. I've done a ton of fundraising. I've been on these amazing fundraising expeditions and made incredible friendships. In some ways, it has enhanced my life. I can't lie about it. It's not just this tragedy. It's like anything in life: It's what you make of it. Making the memories, spending family time, telling people close to me how I feel about them, not leaving any stone unturned—those are all good ways of living. We're all refractory patients if you're in the myeloma journey. I mean, it's just—you can't avoid that. And yeah, I would say lean on others, get involved, and ask for help if you need it. And once you are around for a little while, offer help to others and be a mentor.

Mary DeRome (MMRF): This has been a really fantastic conversation, and I would like to once again thank our panelists today, John Bush, David Franks, and Mark Hercart for their time and for their stories.

Narrator: Thank you for listening to this episode of the *Myeloma Matters* podcast on relapsed and refractory multiple myeloma, hosted by the Multiple Myeloma Research Foundation. The MMRF thanks David Franks, John Busch, and Mark Herkert for sharing their stories and unique perspectives on myeloma relapse. The MMRF also thanks AbbVie, BMS, CURE, Genentech, GSK, Janssen, Karyopharm, Sanofi and Takeda Oncology for their generous support of this podcast. If you have additional questions about what you heard today, please call the MMRF Patient Navigation Center at 1-888-841-6673.

If you’ve enjoyed this series, be sure to leave a comment or review wherever you get your podcasts.